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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/764,359	01/19/2001	Lola M. Reid	320727.50601	7133
22428 7590 01/29/2008 FOLEY AND LARDNER LLP SUITE 500 3000 K STREET NW WASHINGTON, DC 20007			EXAMINER NGUYEN, QUANG	
			ART UNIT 1633	PAPER NUMBER
			MAIL DATE 01/29/2008	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**Advisory Action  
Before the Filing of an Appeal Brief**

Application No.

09/764,359

Applicant(s)

REID ET AL.

Examiner

Quang Nguyen, Ph.D.

Art Unit

1633

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 08 January 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☒ The Notice of Appeal was filed on 02 October 2007. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: \_\_\_\_\_.  
Claim(s) objected to: \_\_\_\_\_.  
Claim(s) rejected: 1,3,4,6-9,12-21 and 23-34.  
Claim(s) withdrawn from consideration: \_\_\_\_\_.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☒ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_.  
13. ☐ Other: \_\_\_\_\_.

Continuation of 11. does NOT place the application in condition for allowance because: Applicants' arguments are respectfully not found persuasive to overcome the rejections of record for reasons discussed below.

Once again, Applicants argue that Reid only teaches the isolation of liver cells from embryonic and neonatal livers immediately post-mortem, and the examiner interprets the isolation of hepatoblasts from any age from any species taught by Reid to include 2 hours and 30 hours after death. With respect to secondary references, Faris only teaches the isolation of cells immediately following anesthetization of the donor, although the examiner notices that Faris professes that the isolation method may be performed on "mammalian organ donors including deceased donors or cadavers"; while Brasile is silent on stem cells altogether. Accordingly, these references alone or in combination do not teach or suggest a method of isolating liver progenitor cells from a liver tissue obtained between about 2 hours and 30 hours postmortem. Furthermore, Applicants argue that the presently claimed invention was completely unexpected since all known prior art references regarded ischemically damaged organs as being totally useless for any meaningful purpose and that the present inventors were the first to take advantage of the discovery that progenitors were actually resistant to ischemia. An ordinary skilled artisan would not have expected any success in isolating progenitor cells from tissue greater than about 2 hours postmortem because the scientific community assumes that the liver autolyzes within less than an hour, and that progenitor cells being particularly sensitive to ischemic damage would be the first cells to die.

1. With respect to the Reid reference, the examiner does not interpret the isolation of hepatoblasts from any age from any species taught by Reid to include 2 hours and 30 hours after death as argued by Applicants. If this is the Examiner's interpretation, the examiner would not need the supplemental teachings of Faris and Brasile to make the 103 rejection of record.

2. Whether Applicants like it or not, Faris explicitly disclosed that a population of liver stem cells from adult liver tissues from various species such as a mouse, a pig or a human can be isolated from liver tissues obtained from mammalian organ donors, including deceased donors or cadavers (col. 5, lines 3-25). Thus, Applicants are not the first to recognize that liver stem cells can be isolated from liver tissues obtained at least 2 hours postmortem or liver progenitors are resistant to ischemia. Moreover, the teachings of Faris are opposite to Applicants' argument that the scientific community assumes the liver autolyzes within less than an hour and that liver progenitors are particularly sensitive to ischemic damage. Furthermore, Brasile already discloses at least a process for inducing repair of livers deprived of blood flow for between about 0.5 to 4 hours by flushing and perfusing the livers for approximately 2 hours for resumption of organ function by overcoming the effects of warm ischemia. Once again, the teachings of Brasile proved that liver tissues obtained at least 2 hours post-mortem are not totally useless for any meaningful purpose as argued by Applicants.

3. As already stated in the 103 rejection of record, it would have been obvious for an ordinary skilled artisan to modify the teachings of Reid by also obtaining liver tissues from deceased donors or cadavers for the preparation of hepatoblast cell populations and that these liver tissues should be obtained as fresh as possible to avoid cell death in the harvested tissues caused by warm ischemia that ensues rapidly upon death, including the use of liver tissues deprived of blood flow for between about 0.5 to 4 hours but subjected to the treatment of flushing and perfusion for about 2 hours to regain organ function and without any further tissue damage as taught by Brasile.

4. There is nothing unexpected or surprising or unpredictability with respect to the totality of the teachings of Reid, Faris and Brasile as discussed above.

5. It is further noted that the Declaration of Dr. Neil Theise under 37 CFR 1.132 filed on 01/08/08 was not considered by the Examiner for the reason indicated in item 9 above.

6. With respect to the obviousness-type double patenting rejection, Applicant's same arguments are also not found persuasive for the reasons discussed in the preceding paragraphs.

  
QUANG NGUYEN, PH.D.  
PRIMARY EXAMINER